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Information and Discussion Topics for HEI Research Committee

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Bruce Copley, MPH, PhD
Senior Epidemiology Associate
ExxonMobil Biomedical Sciences, Inc. (EMBSI)

Overview

Industry-Sponsored PM Causal Symposium

Spirometry and Oscillometry Variability (SOLVe) Study

Comments/Suggestions on Research

Questions?

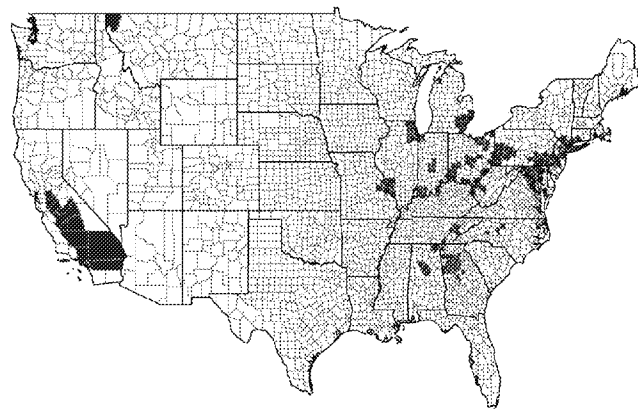
Causal Symposium on Particulate Matter

Symposium on Causal Methods in Epidemiological Studies of Particulate Matter and Mortality

- Objective: Assess causal relation between PM & mortality using appropriate study designs
- Approach: Research teams received same 'regression-ready' Medicare & PM dataset to answer investigator-determined causal questions
- Selection/Awards: Top 3/11 proposals via RFP selected by special panel (F. Dominici, Harvard; S. Greenland, UCLA; A. Rappold, EPA); funded by Industry Consortium
 - **Causal Estimates of the Relationship between Fine Particulate Matter and Mortality using Attainment Status under the Clean Air Act Amendments** (Matt Neidell, Columbia University; Nicholas Sanders, Cornell University; Alan Barreca, UCLA)
 - **The Impact of PM_{2.5} on Mortality—Evidence from a Natural Experiment: Closure or Unit Shut-down of Coal-fired Power Plants** (Yi Wang, Indiana University; Maoyong Fan, Ball State University)
 - **A Counterfactual Approach to Quantify the Causal Effect of Fine Particulate Matter on Mortality Using a Novel Approach** (Zhengyuan Zhu and Zhulin He, Iowa State University; Richard Smith, University of North Carolina at Chapel Hill)
- Symposium held 3-4 October at UNC-Chapel Hill Rizzo Center

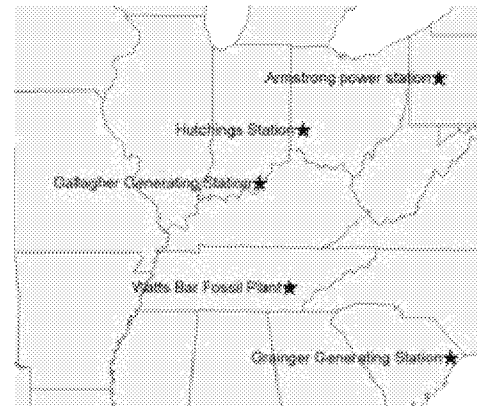
Causal Estimates of the Relationship between PM2.5 and Mortality using Attainment Status (Neidell, Sanders, & Barreca)

- QE/Accountability study of implementation of 1997 PM2.5 NAAQS and its effect on all-cause LT mortality (attainment vs non-attainment counties); pre-/post-2005
 - *Did the NAAQS effect PM2.5 levels?*
 - *Did the NAAQS reduce mortality?*
- Basic difference-in-differences analytical method reveals causal impact of PM2.5 *policy*, not PM2.5 itself
- Analytical enhancements and robustness checks designed to assess *PM2.5* causality
 - Additional control variables: meteorological elements, economic variables, migration
 - “Event study” analysis to rule out differential trending in treatment (non-attainment) and control (attainment) counties in mortality prior to treatment (i.e., before 2005)
 - “Nearest neighbor” county matching based on propensity scores



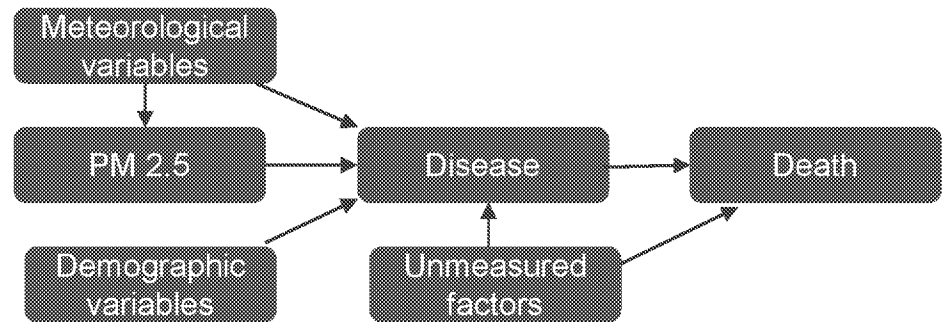
Impact of PM_{2.5} on Mortality—Evidence from a Natural Experiment: Retirement of Coal-fired Power Plants (Wang & Fan)

- QE/Intervention study impact of coal-fired power plant retirement or unit shutdown (on short-term all-cause mortality, 2009–2013; N = 5)
 - Exclusions: Spatially-clustered plants; small plants < 50 MW/day; plants with installed scrubbers
 - “Treated” counties: location of power plant and those within 50 km radius downwind of plants
 - “Control” counties: “similar” counties matched 1:10 on several covariates to treated counties; excluded all non-treated counties within 50 km radius
 - Supplemented data collection with econometric data
- Differences-in-difference instrumental variable (plant retirement using exact retirement dates for the ‘intervention’) analytical approach to estimate causal effect of PM reduction



A Counterfactual Approach to Quantify the Causal Effect of PM2.5 on Mortality Using a Novel Approach (Zhu & He)

- Statistical modeling approach using a structural nested mean model to better control for time-varying confounding
 - Model not previously applied to air pollution epidemiologic research
 - Permitted assessment of regional heterogeneity of PM2.5 impact on short-term mortality
- Mortality age-weighted by CDC data to account for “rate inflation” via aging over the period
- Novel causal model adjusted by strong assumptions on unmeasured factors
- Compared results against two traditional (non-counterfactual) time-series models



General Reviewer Comments (and Author Concerns)

- Critical need for focused causal (inference) research in air pollution epidemiology
- Use caution in labeling studies as “causal” (just saying so isn’t enough); causal inference framework needs continued development/refinement
- Causal studies should be considered along with traditional associational studies to increase confidence in those results and provide additional insight to inform causal conclusions
- Study designs and analytical methods were appropriate to answer causal questions but still had untestable or “partially verified” assumptions that limit causal interpretation
 - Effect on mortality might be due to changes in other pollutants
 - Stable unit treatment value assumption (SUTVA)
 - “Spillover” effects from pollution control activities into neighboring counties
 - Differing attainment strategies; different timing of implementation/control measures
 - Different pollutants/emissions between treatment & control counties → differential toxicity and health impacts

Spirometry and Oscillometry Variability (SOLVe) Study

Objective: Compare Methods for Quantifying Lung Function

Determine which method produces the least short-term intra- and inter-visit variability, *independent of exposure*

- Current methods don't fully consider intra-session and/or inter-session variability in individuals
- Accounting for this variability could influence statistical interpretation in research settings

Spirometric Reporting Options (FVC and FEV1)
1. Largest single value (current ATS/ERS Criteria)
2. Mean of 3 largest values
3. Mean of all maneuvers
4. Largest from maneuver with highest peak flow

Oscillometric Reporting Options (R & X @5 & 20Hz; R5-R20; RA @ 5 Hz)
1. Mean of 3-5 maneuvers
2. Mean of 3 maneuvers within 10%
3. Mean of all maneuvers
4. Largest single value

Oscillometry parameters: resistance (R), reactance (X) at 5 & 20 Hz, frequency dependency of resistance (R5-R20) reactance area at 5 Hz (AX5)

- PI: Dr Mike Falvo (Rutgers); Rutgers IRB & EM Research Ethics Committee approved
- Funding & Project Oversight: EPRI (managing), API, EMBSI
- ESAC: Chang (Emory), Schelegle (UC-Davis), Frampton (Rochester), Kim (EPA)

Forced Oscillation Technique (FOT, aka “Oscillometry”)

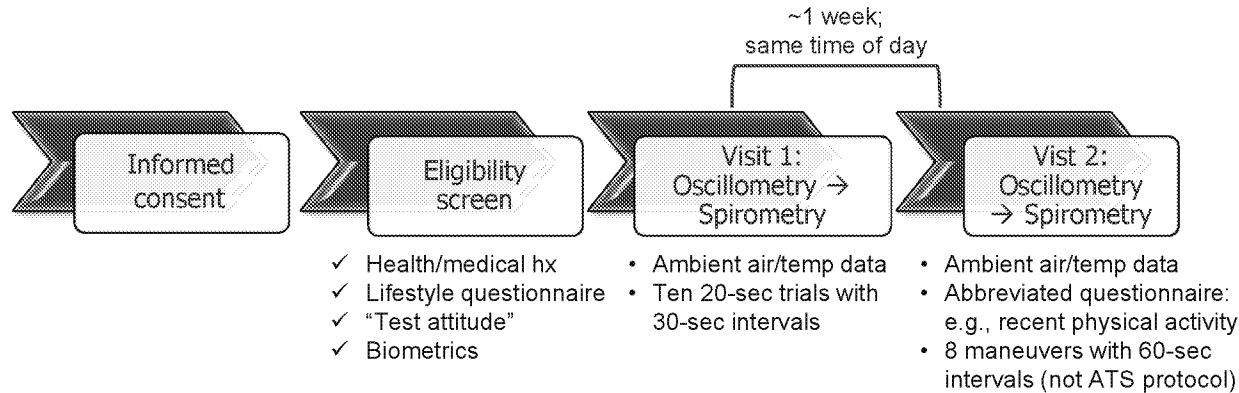
- Not effort-based; test performed at tidal volume (normal breathing)
- Developed relatively recently; used primarily in Europe but slowly increasing in US
 - Primary tool for evaluating respiratory effects of occupational exposures
 - More sensitive assessment of distal airways vs. spirometry
- Clinical practice guidelines established by European Respiratory Societies (ERS), but rationale lacking
- Near absence of FOT data to assess measurement error and selection of variables
- Additional research needed to fill data gaps; also need to compare against spirometry



Photo courtesy of Dr Mike Falvo, US Veterans Administration, with consent from the individual (non-patient) in the photo.

SOLVe Study Design

- Observational study of healthy adults, ages 18-40 yrs; N = 100; no controlled exposure
- After rolling recruitment to ensure equal representation of both sexes and age range . . .



- Recruitment underway; ECD for complete data collection: mid-/late 2020
- Presentations and peer-reviewed publication of results
- Workshop/symposium on impact of findings on interpretation of PFT results in research settings, not clinical!

HEI Research Activities

HEI's "Third Wave" Accountability Research Plan

1. **Long-term complex regulatory programs:** studies that evaluate regulatory and other actions at the national or regional level implemented over multiple years
 2. **Interventions at the local level:** studies that evaluate actions targeted at improving air quality in urban areas (e.g., diesel bans)
 3. **Ports and global transport:** studies that evaluate regulatory and other actions to improve AQ around major ports (both marine and air) & transportation hubs/corridors
 4. **Methods development and dissemination:** studies that develop, apply and disseminate statistical and other methodology for conducting such research
- **Recommendation:** Proposals which include *quantitative bias analysis* be rewarded during review process
 - Systematic errors (biases) are primary threat to validity in the large epidemiology studies
 - Not to be conflated with sensitivity or risk of bias analyses
 - Consistent with HEI's overarching methodological development objectives

Susceptibility to Multiple Air Pollutants in CVD

- Uses a much-needed deprivation index, a robust measure of socioeconomic status/position
 - Limited to NYC, but provides a model for future research (?)
 - Improvement over the typical individual income and/or educational attainment variables
 - Adds to the commonly used Census-based data on neighborhood characteristics including under-researched community stressors
- Targets effect measure modification in pollutant-disease statistical association
- Presents an opportunity to also better assess confounding by SES since . . .
 - several studies have shown higher PM concentrations in low SES areas (e.g., Crouse et al. 2012; Hoek et al. 2013; Hajat et al. 2015), *and*
 - a *Lancet* meta-analysis of 48 prospective cohort studies: low SES had CVD mortality HR = 1.29 (95% CI: 1.16-1.43); low SES-related behaviors even higher (Stringhini et al. 2017).
 - Recommend follow-on work to determine appropriate unit of analysis to address 'modifiable areal unit problem' (MAUP), i.e., different units of analysis generate contradictory findings

US Low-Level PM Study

- Observational study with defined cohort (Medicare)
- Robust set of analytical requirements taking up to 3 years to complete
- Not a clinical trial, but . . .
 - “**Preliminary** analysis” published in NEJM (2017)
 - Upcoming analysis (‘**interim**’) under special HEI review; publication near term
 - **Final** results when study is completed with HEI review
- Concerns
 - Preliminary and current findings could differ from final
 - Preliminary/incomplete analysis has staying power
 - “Multiple looks” at data along the way to final
 - Is (administrative) Medicare data sufficiently “research grade” for meeting NAAQS research needs?

Energy Research Program

- Focus area is potential population exposures and health effects from onshore unconventional oil and gas development (OGD) in the US
- Modeled on HEI's air program (e.g. governance, balanced-funding) to deliver high-quality, impartial science that informs current & future public policy decisions
- Year one completed: Energy Research Committee established; scoping meeting and two exposure & risk screening workshops conducted
- Key pending milestones
 - Anticipated release of year one technical work products (reports and papers)
 - Health effects literature review
 - Exposure literature review and identification of research to address important knowledge gaps
 - Results will help to shape research solicitation (in the form of a RfQ)
 - Confirmation of government (EPA) funding

Questions or Comments?

Thank you



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